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**From:** White, Paul [White.Paul@epa.gov]  
**Sent:** 5/27/2014 3:43:27 PM  
**To:** Strong, Jamie [Strong.Jamie@epa.gov]; Newhouse, Kathleen [Newhouse.Kathleen@epa.gov]  
**CC:** Gehlhaus, Martin [Gehlhaus.Martin@epa.gov]  
**Subject:** RE: Draft of BaP dermal bioavailability table

Kathleen and Jamie,

Thanks for the request. I will look at and get back within the next couple days. (Today I'm trying to help with a question with the vanadium assessment.)

I pulled some additional studies with BAP bioavailability and dosimetry related data, so I may also suggest a few references to cite.

Paul

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**From:** Strong, Jamie  
**Sent:** Thursday, May 22, 2014 7:55 AM  
**To:** Newhouse, Kathleen; White, Paul  
**Cc:** Gehlhaus, Martin  
**Subject:** RE: Draft of BaP dermal bioavailability table

Paul,  
It would be great if you would take a look at this response for us.  
Thanks,  
Jamie

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**From:** Newhouse, Kathleen  
**Sent:** Wednesday, May 21, 2014 6:40 PM  
**To:** White, Paul  
**Cc:** Strong, Jamie; Gehlhaus, Martin  
**Subject:** FW: Draft of BaP dermal bioavailability table

Hi Paul, I will be out of the office until June 2<sup>nd</sup>. If you have any edits to this or other thoughts in the meantime, please send them to Jamie Strong and Martin Gehlhaus.

Thanks,  
Kathleen

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**From:** Newhouse, Kathleen  
**Sent:** Monday, May 05, 2014 5:50 PM  
**To:** White, Paul; Hogan, Karen  
**Cc:** Strong, Jamie; Gehlhaus, Martin  
**Subject:** RE: Draft of BaP dermal bioavailability table

Hi Paul, thanks for chatting with me about interspecies toxicokinetic differences. Here is the comment and response that I have drafted. Please let me know if you have some ideas for beefing up the response.

Thanks,  
-Kathleen

Comment: **Cross-species extrapolation of dermal slope factor.** *Several commenters indicated that differences between mouse and human skin should be recognized and accounted for in the calculation of the dermal slope factor for skin*

cancer. Specifically, the commenter stated mouse skin is thinner and more permeable to B[a]p, aryl hydrocarbon hydroxylase inducibility is 40-75 times higher in mice, mouse skin produces more BaP-diol epoxide metabolites, and that DNA-adducts are formed at higher rates in mouse skin and repaired at lower rates relative to human skin. Another commenter recommended increased discussion of the uncertainty regarding the method for interspecies scaling of the dermal slope factor.

## Ex. 5 Deliberative Process (DP)

**From:** Newhouse, Kathleen  
**Sent:** Thursday, April 24, 2014 11:45 AM  
**To:** White, Paul; Hogan, Karen  
**Cc:** Strong, Jamie; Gehlhaus, Martin  
**Subject:** RE: Draft of BaP dermal bioavailability table

Hi Paul, I was wondering whether you have had time to think about the issue of this issue of quantitative differences between mouse and human skin and which ones you think would be expected to scale with BW<sup>3/4</sup>.

I am working to address some public comments (see below). They cite Crump (2000), and I will attach, but this is a report generated by TERA and "published" on their website. So I would take it with a grain of salt.

Ex. 5 Deliberative Process (DP)

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Here are some of the public comments:

### 4. Differences between human skin and mouse skin

There is nothing wrong with relying, as the *Draft Review* does, on the results of skin painting studies in laboratory mice for purposes of human health risk assessment. However, this reliance should be accompanied by explicit recognition of, and accounting for, the important biological differences between the skin of the mice and the skin of humans.

These differences (highlighted in Crump, 2000, discussed below) include the following.

- Mouse skin is thinner and more permeable to B[a]p and related PAHs than is human skin (Reifenrath *et al.*, 1984; Crump, 2000).
- B[a]p and related PAHs induce the activity of the important, activating enzyme aryl hydrocarbon hydroxylase (AHH) in both mice and humans, but the inducibility of AHH is some 40-75 times higher in mouse skin relative to human skin (Crump, 2000).
- B[a]p is transformed into the genotoxic metabolite 7,8-9,10-dihydrodiol epoxide — BPDE— in both mice and humans, but, at comparable B[a]p doses, mouse skin apparently produces considerably more of this metabolite than does human skin (as discussed below; also, Crump, 2000).

- B[a]p and related PAHs can induce DNA damage (*via* DNA-adducts) in both mice and humans, but these adducts are formed at higher rates in mouse skin relative to human skin; and the resulting damage is repaired at lower rates in mouse skin relative to human skin (reviewed in Crump, 2000).

Thanks for any insight you can provide!

Kathleen

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**From:** White, Paul  
**Sent:** Friday, February 28, 2014 2:21 PM  
**To:** Newhouse, Kathleen; Hogan, Karen  
**Subject:** RE: Draft of BaP dermal bioavailability table

Hi Kathleen,

I'll give this a little thought and get back to you.

Paul

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**From:** Newhouse, Kathleen  
**Sent:** Friday, February 28, 2014 1:17 PM  
**To:** White, Paul; Hogan, Karen  
**Subject:** RE: Draft of BaP dermal bioavailability table

Paul, thanks for working on this.

So, I have a tangential question since you have looked at many of the dermal absorption papers for BaP:

Ex. 5 Deliberative Process (DP)

## Ex. 5 Deliberative Process (DP)

-K

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**From:** White, Paul  
**Sent:** Friday, February 21, 2014 2:03 PM  
**To:** Hogan, Karen; Newhouse, Kathleen  
**Cc:** White, Paul  
**Subject:** Draft of BaP dermal bioavailability table

Hi. I've been happy to try and sort out a couple of the BaP dermal bioavailability issues that Karen mentioned to me. Per our previous conversations and emails,

Ex. 5 Deliberative Process (DP)

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This table needs a bit of work – and checking for errors – prior to any use. I will try to clean this up shortly as well as draft some brief text to explain. But thought I'd share as I know you are trying to sort out things quickly...

Paul